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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

P960005

Date SEP - 9 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of the Dade International, Incorporated's aca® *plus* PSA Test Kit, the aca® *plus* PSA Calibrator and the aca® *plus* PSA Control - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Doreen M. Melling, CDRH, HFZ-402, 8/22/96, 594-2186

DRAFT

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[DOCKET NO. _____]

Dade Intl., Inc.; Premarket Approval of the aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Dade Intl., Inc., Newark, DE, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator, and aca® ***plus*** PSA Control. FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on September 9, 1996, of the approval of the application. DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., Rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Peter E. Maxim, Ph.D.,

Center for Devices and Radiological Health (HFZ-440),

Food and Drug Administration,

2098 Gaither Rd.,

Rockville, MD 20850,

301-594-1293.

SUPPLEMENTARY INFORMATION: On February 1, 1996, Dade Intl., Inc., Newark, DE, 19714, submitted to CDRH an application for premarket approval of the aca® ***plus*** Test Kit, aca® ***plus*** PSA Calibrator, and aca® ***plus*** PSA Control. The device is a Prostate Specific Antigen (PSA) Test Kit, which consists of the PSA test pack and reaction vessel used in the aca® ***plus*** immunoassay system to quantitatively measure PSA in human serum. Measurements of PSA are used as an aid in the management of prostate cancer patients. In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Immunology Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

On September 9, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Ms. Rebecca S. Ayash
Dade International, Inc.
Route 896
P.O. Box 6106
Newark, Delaware 19714

SEP - 9 1996

Re: P960005
. aca® *plus* PSA Test Kit, aca® *plus* PSA Calibrator, and aca® *plus* PSA Control
Filed: February 1, 1996
Amended: May 1, May 7, May 17 and May 30, June 7, August 12, September 3, and September 4, 1996

Dear Ms. Rebecca S. Ayash:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the aca® *plus* PSA Test Kit, aca® *plus* PSA Calibrator, and the aca® *plus* PSA Control. The device is a Prostate Specific Antigen (PSA) Test Kit, which consists of the PSA test pack and reaction vessel used in the aca® *plus* immunoassay system to quantitatively measure PSA in human serum. Measurements of PSA are used as an aid in the management of prostate cancer patients. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution and use of this device are restricted to prescription use in accordance with 21 CFR 801.109.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for the aca® *plus* PSA Test Kit has been established and approved at 12 months at 2° to 8° C. Expiration dating for the aca® *plus* PSA Calibrator and Control has been established and approved at 6 months at 2° to 8° C. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is

publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Peter E. Maxim, Ph.D. at (301) 594-1293.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

4

I. GENERAL INFORMATION

Device Generic Name:

Immunoassay system to quantitatively measure prostate specific antigen (PSA) in human serum.

Device Trade Name:

aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator, aca® ***plus*** PSA Control

Applicant's Name and Address:

Dade Intl., Inc.
Route 896
P.O. Box 6106
Newark, DE 19714

Premarket Approval (PMA) Number:

P960005

Date of Panel Recommendation:

Pursuant to section 515 (c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Immunology Devices Advisory Panel meeting because the information in the PMA substantially duplicates information previously reviewed by this Panel.

Date of Notice of Approval to the Applicant: SEP - 9 1996

II. INDICATIONS FOR USE

Intended Use

The PSA test pack and reaction vessel are used in the aca® ***plus*** immunoassay system to quantitatively measure prostate specific antigen (PSA) in human serum. Measurements of PSA are used as an aid in the management of prostate cancer patients.

Contraindications, Warnings and Precautions

Contraindications:
There are no known contraindications for the aca® ***plus*** PSA Test Kit.

Warnings and Precautions:

Warnings and Precautions:

Warnings and Precautions for use of the device are stated in the attached product labeling (Attachment A).

Background:

Prostate specific antigen (PSA) is a serine protease of approximately 30,000 Daltons produced by the epithelial cells of the prostate gland.[1,2] PSA is found in high concentrations in seminal fluid and serves to liquefy the seminal coagulum.[3] The level of PSA in serum and other tissues is normally very low. In malignant prostate disease (prostatic adenocarcinoma) and in non-malignant disorders such as BPH and prostatitis, the serum level of PSA may become elevated.[4,5,6,7] The specificity of PSA to prostate tissue makes it a significant marker for use as an aid in the management of prostate diseases.

Serum levels of PSA are most useful when sequential values are monitored over time. Monitoring is typically done on a weekly or monthly basis, as the serum half-life of PSA is 3 to 4 days.[8] After complete removal of the prostate gland (radical prostatectomy), PSA levels should decline to a very low or undetectable level. A rise of the serum PSA level in prostatectomy patients indicates residual prostate tissue, recurrence, or metastasis of the disease.[9] Serum PSA levels during radiation treatment should decline and remain at baseline while the patient is in remission.[10]

Recent research has demonstrated that most of the PSA protein in serum is complexed with either α1-antichymotrypsin (ACT) or α-2-macroglobulin.[11,12] The PSA protein associated with α-2-macroglobulin is encapsulated and unavailable for measurement by currently marketed immunoassays. About 90 percent of the measurable PSA in serum exists as PSA-ACT complex and about 10 percent is free. The aca® ***plus*** PSA Test Kit is standardized with PSA-ACT and measures both the free and ACT bound components of serum PSA.

III. DEVICE DESCRIPTION AND PRINCIPLE OF THE ASSAY

The aca® ***plus*** PSA Test Kit is a solid phase two-site, one-step immunoenzymetric assay designed for use on the aca® immunoassay system. The aca® ***plus*** immunoassay system is a fully automated random access analyzer consisting of an aca® ***plus*** PSA Test Kit and an aca® discrete clinical analyzer. The aca® ***plus*** immunoassay system performs the pretreatment step using an aca® ***plus*** PSA Test Kit reaction vessel. The PSA reaction vessel contains a mouse monoclonal antibody immobilized on chromium dioxide particles (capture antibody) and a second mouse monoclonal antibody fragment [F(ab')2] conjugated to the enzyme, β-galactosidase (tag antibody). The PSA sample is

automatically added to the PSA reaction vessel and mixed by the aca® ***plus*** immunoassay system. PSA in the sample reacts with the capture and tag antibodies to form a chrome-capture antibody-PSA-conjugate complex (sandwich). Unbound conjugate and residual sample components are removed during wash steps automatically performed by the aca® ***plus*** immunoassay system.

The complex is then quantitatively transferred to an aca® ***plus*** PSA analytical test pack. The test pack must be transferred by the operator to an aca® analyzer for quantitation within two hours after processing by the aca® ***plus*** PSA Test Kit. The PSA pack contains the chromogenic substrate chlorophenol red-β-D-galactopyranoside (CPRG) and HEPES buffer. The bound β-galactosidase on the chrome complex catalyzes the hydrolysis of CPRG to chlorophenol red (CPR). The color change measured by the aca® discrete clinical analyzer at 577nm due to the formation of CPR which is proportional to the concentration of PSA present in the patient sample.

In addition to the aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Controls are required to perform the assay. The aca® ***plus*** PSA Calibrator is a three level liquid product, packaged and sold separately from the aca® ***plus*** PSA Test Kit. The product is used to calibrate the aca® ***plus*** immunoassay system to assure accurate results over the assay range of the method. The calibration curve generated during system calibration is automatically stored by the aca® ***plus*** immunoassay system. The aca® ***plus*** PSA Control is a two level, liquid quality control material also sold separately from the aca® ***plus*** PSA Test Kit. The aca® ***plus*** PSA Control is to be tested at least once daily to monitor system performance.

IV. ALTERNATE PRACTICES AND PROCEDURES

Several alternate practices and procedures are used by physicians for management and monitoring of patients with prostate cancer.[13,14] These include, but are not necessarily limited to, the following:

- Serum levels of total acid phosphatase
- Serum levels of total alkaline phosphatase
- Serial determination of serum prostatic acid phosphatase
- Serum levels of bone alkaline phosphatase
- Imaging modalities such as x-ray and/or magnetic resonance Ultrasonography
- Lymphangiography and/or lymphadenectomy

These practices and procedures are used to assess possible metastasis of the prostate cancer to the regional lymph nodes or distal sites, including bone.

V. MARKETING HISTORY

The aca® ***plus*** PSA immunoassay test kit, aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control have not been previously marketed.

VI. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Any adverse effects of the device on health would be indirect, since the device does not come in contact with the patient.

An erroneous result by this test could adversely affect the management of a patient. A falsely low result may delay beneficial treatment in cases of recurring or progressing cancer. A falsely elevated PSA result may trigger further investigation by alternate procedures and lead to needless therapy.

VII. SUMMARY OF STUDIES

1. Nonclinical Laboratory Studies

Characterization of Cell Lines and Antibodies

Cell lines for the capture and tag of monoclonal antibodies used in the aca® ***plus*** PSA immunoassay system were selected on the basis of reactivity with PSA-ACT in serum and the ability to inhibit binding of antibodies to PSA in a device for which there is an approved PMA (the PSA reference device).

Purified antibody was characterized by isoelectric point (pI), isotype and subtype, and specific activity. Testing to assess specificity of the antibodies included specific inhibition of PSA from a similar PSA reference device using both free PSA and PSA-ACT complex and Western Blot analyses with sera from patients known to have prostate cancer. These studies indicated that the antibodies were specific to PSA.

Characterization of PSA-ACT

The purified PSA-ACT complex used in the aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control is manufactured by Dade International, Inc., and was characterized relative to The National Committee for Clinical Laboratory Standards (NCCLS) protocol I/LA19-P. [16]

The PSA-ACT complex was characterized in terms of endogenous PSA enzymatic activity, purity by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) under reducing conditions, and structural integrity based on Western Blot analyses. Amino acid analyses and molecular weight by mass spectroscopy were performed to further characterize the complex.

No enzymatic activity of the PSA-ACT complex was observed indicating that PSA was completely bound with ACT. SDS-PAGE and Western Blot analyses demonstrated acceptable purity and homogeneity. Amino acid analysis demonstrated nearly identical results to published values. Molecular mass for PSA-ACT complex was consistent with the molecular masses of the PSA and ACT raw material in that the complex contained one PSA and one ACT molecule.

Performance Characteristics

1. Reproducibility Studies

Intra-Assay Variation (Within-run Reproducibility)
Intra-assay variation (within-run reproducibility) was evaluated by repeated measurements of five serum pools of different PSA concentrations and both levels of aca® ***plus*** PSA Control. Each sample was assayed thirty times in one independent run. The mean, standard deviation (SD), 95 percent confidence interval of the SD, and coefficient of variation (CV) were determined for each sample. Precision was observed over the concentration range tested. CV's from 1.5 to 3.4 percent at PSA concentrations in the range of 3.5 to 78.0 ng/mL were observed. A CV of 17.5 (SD of 0.08 ng/mL) was observed for a PSA concentration of 0.5 ng/mL.

Inter-Assay Variation
Inter-assay variation was evaluated using the same serum pools and controls used in the intra-assay study. Each sample was assayed in duplicate once a day for 20 days. The data were analyzed using an Analysis of Variance (ANOVA) technique to determine estimates of within-run and total reproducibility for each sample. The mean and the standard deviation, 95 percent confidence interval of the SD, and CV for each reproducibility term were determined for each sample. CV's from 2.0 to 3.2 percent for PSA concentrations of 3.5 to 77.0 ng/mL were observed. A CV of 21.5 (SD of 0.11 ng/mL) was observed for a PSA concentration of 0.5 ng/mL. CV's of the reproducibility results are presented in Table 1.

Table 1: Inter-Assay variation (Total Reproducibility)

Serum Pool	Mean PSA Value ng/mL	Within-Run %CV	Total %CV
1	0.49	21.5	21.5
2	3.46	3.1	3.2
3	9.50	1.3	2.1
4	39.70	1.9	2.3
5	76.53	1.6	2.0
aca® *plus* PSA Control			
L1	4.19	2.9	3.1
L2	46.00	2.1	2.1

Lot-to-Lot Variation

Lot-to-lot variation of three aca® ***plus*** PSA Test Kits were evaluated by assaying 100 serum samples with PSA values distributed across the assay range of the method. A different aca® ***plus*** PSA Calibrator lot was used to calibrate each aca® ***plus*** PSA Test Kit lot on the aca® ***plus*** immunoassay system. Agreement was demonstrated between the lot combinations tested as shown by the regression statistics summarized in Table 2. Correlation of PSA values <10 ng/mL is presented in Table 3.

Table 2: aca® ***plus*** Lot-to-Lot Variation
aca® ***plus*** PSA Lot Combination 1

PSA Lot Combination	n	Slope	Intercept	Sy,x	Correlation Coefficient
2	100	0.990±0.010	0.99±0.47	2.60	0.9957
3	100	0.998±0.013	1.10±0.64	2.57	0.9921

Table 3: aca® ***plus*** Lot-to-Lot Variation
aca® ***plus*** PSA Lot Combination 1
PSA Values <10ng/mL

PSA Lot Combination	n	Slope	Intercept	Sy,x	Correlation Coefficient
2	18	1.02±0.02	0.09±0.07	0.24	0.9969
3	17	0.99±0.02	0.20±0.05	0.17	0.9978

14

Lot-to-lot variation also was assessed by testing each of three lots of aca® ***plus*** PSA Test Kits with three aca® ***plus*** PSA Control lots and serum pool with an approximate PSA value of 0.5ng/mL. Pooled between lot CV for aca® ***plus*** PSA Control are listed in Table 4. Equivalent values were obtained across all three aca® ***plus*** PSA Test Kits.

Table 4: aca® ***plus*** Lot-to-Lot Variation between Lot CV

aca® ***plus*** PSA Control	Mean ng/mL	% CV
Level 1	4.3	3.7
Level 2	47.4	0.0

Interlaboratory Variation

Interlaboratory variation was assessed across six different laboratories. The laboratories that participated in the study were:

Site 1	Johns Hopkins Hospital
Site 2	M.D. Anderson Cancer Center
Site 3	University of Alabama at Birmingham
Site 4	Lab 240, DuPont Glasgow Research Laboratory
Site 5	Lab 242, DuPont Glasgow Research Laboratory
Site 6	Technical Support Laboratory, DuPont Business Community

Five serum pools (SP) with PSA concentrations spanning the assay range of the method and aca® ***plus*** PSA Control were used in the study. All laboratories used the same lots of aca® ***plus*** Test Kits, aca® ***plus*** PSA Calibrator, and aca® ***plus*** PSA Control. Each site assayed ten replicates of each sample in a single run.

The mean, SD and CV for within-run, between-lab and total reproducibility were determined for each sample using an ANOVA technique. Interlaboratory coefficients of variations (between-lab) ranged from 1.1 to 9.5 percent. The results for these studies were within acceptable variation for an assay of this type, and are presented in Table 5.

Table 5 Interlaboratory variation

Sample	Mean ng/mL	N	Within-run		Between-Lab		Total	
			SD	%CV	SD	%CV	SD	%CV
SP1	0.48	60	0.08	17.6	0.05	9.5	0.10	20.0
SP2	3.46	60	0.12	3.5	0.11	3.0	0.16	4.6
SP3	9.42	60	0.32	3.4	0.23	2.4	0.40	4.2
SP4	39.84	60	0.64	1.6	0.75	1.9	0.99	2.5
SP5	77.66	60	1.79	2.3	1.12	1.4	2.11	2.7
PSA Control L1	4.16	60	0.13	3.1	0.08	1.9	0.15	3.7
PSA Control L2	45.91	60	1.35	2.9	0.50	1.1	1.44	3.1

Within-Sample Reproducibility

One hundred serum samples with PSA values distributed across the assay range of the aca® ***plus*** PSA method were tested in duplicate to evaluate within-sample precision. Replicate one was plotted versus replicate two. A slope of 0.997, intercept of 0.07 and correlation coefficient of 0.9986 were obtained by least squares linear regression analysis. This supported the use of one replicate for patient serum analysis. The reproducibility observed for these studies is within acceptable limits for an assay of this type.

2. Recovery

Recovery was determined at PSA concentrations spanning the range of the assay. Aliquots of twenty serum samples were spiked with three different concentrations of PSA. Concentrations were measured in triplicate for both the unspiked and spiked samples. Recovery ranged from 94.0 to 106.7 percent with an average recovery of 100.6 percent.

3. Linearity

Assay Range Confirmation

Linearity across the assay range of the aca® ***plus*** PSA Test Kit was confirmed by assaying samples prepared from mixtures of high and low serum pools. PSA concentrations ranged from 0.17 to 121.5 ng/mL. Samples were assayed in replicates of five. The observed values were plotted versus the expected values. A slope of 1.00, intercept of 0.18, and correlation coefficient of 0.9997 were obtained. The linear relationship appeared acceptable by visual evaluation. Linearity was confirmed by least squares linear regression analysis and by testing for lack of fit.

Parallelism

Ten serum samples were each diluted serially with aca® ***plus*** Sample Diluent to obtain multiple dilutions of the same sample with values spanning the method assay range. The aca® ***plus*** Sample Diluent was also analyzed. All samples were assayed in triplicate using the aca® ***plus*** PSA Test Kit. The observed values were plotted versus the expected values for each sample. The linear regression slopes ranged from 0.98 to 1.01, with correlation coefficients all greater than 0.9984. The linearity was determined to be clinically acceptable. The dilution profiles also demonstrated parallel response.

Hook Effect

Hook or prozone effect in the aca® ***plus*** PSA Test Kit was evaluated using samples at PSA concentrations ranging from 7,500 to 50,000 ng/mL. These samples were tested with three aca® ***plus*** PSA Test Kits. No hook effect was observed at PSA concentrations up to 50,000 ng/mL.

4. Interfering Substances

The effect of a panel of potential interfering substances on the aca® ***plus*** PSA Test Kit results were evaluated. Test substances were added to aliquots of serum pools at PSA concentrations of 3.1 to 7.3 ng/mL. The samples were compared to a control sample containing no added substance. Recovery ranged from 90.50 to 105.51 percent for all substances except Dextran 75 (a plasma expander). PSA results were elevated by approximately 24 percent in the presence of 2500 mg/dL Dextran 75. Other substances added did not significantly alter the recovery of PSA indicating these substances do not interfere with the aca® ***plus*** PSA Test Kit. Additional testing of lower concentrations of Dextran 75 was performed to determine where acceptable recovery was observed. Test substances were added to aliquots of serum pools at PSA concentrations of approximately 4.0 ng/mL. The samples were compared to a control sample containing no added Dextran 75. Dextran concentrations ranging from 500 to 2500 mg/mL were tested. Recovery was calculated by dividing the mean of the test results by the mean value obtained for the control and multiplying by 100. Recovery ranged from 104.04 to 124.04 percent. Data indicated that clinically significant interference could be observed with the aca® ***plus*** PSA Test Kit at values above 500 mg/dL. A summary of the Dextran 75 test data is provided in Table 6. Table 7 provides a listing of other compounds that did not interfere with the PSA immunoassay.

Table 6 Interference Study Summary Exogenous Substances Drugs and Metabolites Dextran 75

Substance	Test Concentration	% Recovery
Dextran 75	500 mg/dL	104.04
	1000 mg/dL	112.36
	1500 mg/dL	111.69
	2000 mg/dL	118.65
	2500 mg/dL	124.04

Table 7 Interference Study Summary Anti-androgens and anti-neoplastics compounds

Compounds showing no interference with the PSA immunoassay	Test Concentration
Cyclophosphamide	25 mg/dL
Diethylstilbestrol	0.02 mg/dL
Doxorubicin-HCL	7 mg/dL
Estramustine phosphate	20 mg/dL
Flutamide	1 mg/dL
Finasteride	0.2 mg/dL
Goserelin acetate	0.01 mg/dL
Leuprolide acetate	10 mg/dL
Megestrol acetate	2.4 mg/dL
Methotrexate	396 mg/dL

Although there was no significant interference among the substances tested, three substances, namely IgG= -7%, Protein high= +4%, and Rheumatoid Factor= +5.5% showed a small, but statistically significant interference effect. The interference observed for these studies is within the acceptable limits for an assay of this type.

5. Limitations of Procedure

PSA results are not to be interpreted as absolute evidence of the presence or absence of malignant disease. The obtained PSA value should be used in conjunction with information available from clinical evaluation and other diagnostic procedures.

It is possible that a patient with confirmed prostatic cancer may have serum PSA levels within the range of those observed in the

healthy individual. Elevated PSA levels also can be found in patients with nonmalignant diseases of the prostate along with other adjacent genitourinary tissues.

One-step sandwich immunometric assays are susceptible to a high-dose "hook effect", where an excess of antigen prevents simultaneous binding of the capture and detection antibodies to a single analyte molecule.[17]

6. Analytical Sensitivity

The analytical sensitivity of the aca® ***plus*** PSA Test Kit was determined by assaying Level 1 aca® ***plus*** PSA Calibrator (0 ng/mL) thirty consecutive times at monthly intervals for three months, following the initial run. Three aca® ***plus*** PSA immunoassay test kit lots and aca® ***plus*** PSA Calibrator lots were included in the study. The analytical sensitivity ranged from 0.11 to 0.19 ng/mL with a pooled sensitivity of 0.15 ng/mL. From this data the sensitivity was determined to be less than 0.2 ng/mL.

7. Carryover

Potential sample carryover was evaluated to ensure minimal sample-to-sample contamination. A high serum sample prepared by adding PSA-ACT to normal female serum, was run alternately before and after low serum samples to determine the amount of carryover for the aca® ***plus*** PSA Test Kit. The mean of the low serum samples that followed a high PSA sample was statistically equivalent to the mean of the control samples indicating the aca® ***plus*** PSA Test Kit was free of sample-to-sample carryover effects.

8. Instrument Model Comparison

Correlation, precision and sensitivity studies were used to evaluate the performance of the aca® ***plus*** PSA Test Kit on the following aca® instrument models:

aca® III
aca® IV/SX
aca® V
aca STAR™

Only one aca® ***plus*** PMA Test Kit was used to pretreat all aca® PSA Reaction Vessels and Packs used in the study. Fifty serum pools with PSA values spanning the assay range of the aca® ***plus*** PSA method were tested on each of the aca® models listed. Least squares regression analyses of all instrument combinations

demonstrated excellent correlation. Correlation coefficients ranged from 0.9939 to 0.9981 with slopes of 0.96 to 1.01.

Within-run and total reproducibility of the aca® ***plus*** PSA Test Kit of each of the aca® models included in the study were compared. Two serum pools and aca® ***plus*** PSA Controls were used in the study. Each sample was run in duplicate once a day for 5 days. Statistically equivalent precision was demonstrated between aca® models.

Analytical sensitivity was also evaluated on each of the aca® models included in the study. Level 1 of the aca® ***plus*** PSA Calibrator (0 ng/mL) was assayed thirty times on each aca® model. Sensitivity results ranged from 0.07 to 0.16 and were consistent with the sensitivity claim of the assay of 0.2 ng/mL.

The data demonstrated comparable analytical performance between the aca® III, IV/SX, and aca STAR™ models.

9. Stability

Reagent Stability

A real-time stability study was designed to determine the shelf-life of the aca® ***plus*** PSA immunoassay test kit, aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control. The study included three lots of each product and determination of in-use stability of open vials of calibrator and control through multiple uses. Testing was performed at periodic intervals for product stored at 2-8°C. Least squares regression analyses of test results versus test day was used to estimate the rate of change per day for each sample.

Each test day, five replicates were processed for each of five samples on the aca® ***plus*** immunoassay system. The samples used for the aca® ***plus*** PSA Test Kit study were aliquots of aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control which had been stored frozen at -20°C. aca® ***plus*** PSA Test Kits which had been stored frozen at -20°C were assayed in the aca® ***plus*** PSA Calibrator and the aca® ***plus*** PSA Control stability study. The aca® ***plus*** immunoassay system was recalibrated every 90 days according to the calibration interval determined by the system calibration study.

To evaluate in-use stability of open vials, five vials each of aca® ***plus*** PSA Calibrator and five vials each of aca® ***plus*** PSA Control were used repeatedly over several testing points. An aliquot from each vial was assayed at each test point and the vial returned to 2-8°C storage for subsequent testing at additional test points. Least squares regression analyses of test results versus test day were

used to estimate the rate of change per day for each sample. No recalibration was performed as part of this study.

No clinically significant change was observed in the shelf life studies for the aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator or aca® ***plus*** PSA Control as indicated by least squares regression analysis. Data from the in-use stability of open vials supported multiple use of open vials for the aca® ***plus*** PSA Test Kit for 12 months, aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Controls for 6 months when stored at 2-8°C.

System Calibration Stability

System calibration stability was monitored for 91 days. Five replicates of each calibrator level were analyzed once a week during the testing period. Least squares regression analyses of PSA concentration versus day were performed on each calibrator level to determine the bottle value recovery and drift per day. Linear regression analyses of PSA concentration versus day were performed on the daily values per level of aca® ***plus*** PSA Control.

The change in 91 days of aca® ***plus*** PSA level 1 Calibrator (0 ng/mL) was less than 0.2 ng/mL. The values of the Level 2 Calibrator on day 91 were within 2 percent of the values obtained at day 0. The values of the Level 3 Calibrator on day 91 were within 3.1 percent of the values obtained on day 0. These results supported a 3 month system calibration stability.

2. Clinical Performance Studies

Description of Clinical Studies

Clinical studies of the aca® ***plus*** PSA Test Kit were conducted at three institutions to assess the performance of the assay in a clinical laboratory environment. This included evaluation of the analytical performance and the clinical performance of the assay. The studies were retrospective but included prospectively collected surplus samples. The studies had the following objectives:

- to determine the range of PSA levels in serum of healthy individuals, and patients with non-malignant and malignant diseases
- to evaluate the aca® ***plus*** PSA Test Kits as an aid in the management of patients once cancer of the prostate has been diagnosed
- to compare the values of the aca® ***plus*** PSA Test Kit with those obtained from the PSA reference device

The principal investigators and their respective institutions were:

- Daniel W. Chan, Ph.D., Johns Hopkins Hospital, Baltimore, MD
- Herbert A. Fritsche, Ph.D., M.D. Anderson Cancer Center, Houston, TX
- Glen L. Hortin, M.D., Ph.D., The University of Alabama at Birmingham, Birmingham, AL

Study Population

The clinical studies were performed using 2718 sera from normal subjects and from patients with non-malignant and malignant diseases. In addition, PSA values were determined on serial samples from 149 prostate cancer patients monitored over time. Patients were categorized based on the investigators' laboratory records and patient medical records. The analytical and clinical performance of the PSA reference device were also evaluated using the same samples and results were compared to the aca® ***plus*** PSA Test Kit results. A single lot of aca® ***plus*** PSA Calibrator were used.

Six hundred fifty-three of the samples tested were from apparently healthy individuals. These samples were obtained from 345 males 40 years old or greater, 215 males less than 40 years old, and 93 females. A total of 729 samples from patients with non-malignant diseases and a total of 1336 samples from patients with various malignant diseases, including 913 with prostate cancer were included in the study.

The non-malignant disease category included 425 samples from patients diagnosed with BPH, 35 samples from patients with prostatitis, 60 samples from patients with benign hepatic disease, and 121 samples from patients with miscellaneous benign genitourinary disease, including bladder, ureter, orchitis and non-specific benign genitourinary disease.

Of the 913 samples from patients diagnosed with prostatic carcinoma, 127 were Stage A, 300 were Stage B, 211 were Stage C, and 275 were Stage D.

Four hundred and twenty-three samples were from patients with non-prostate malignancies, including genitourinary, gastrointestinal, and pulmonary carcinomas.

Analytical Performance

The analytical performance of the aca® ***plus*** PSA Test Kit was evaluated to assure that the performance observed was consistent with that observed in the nonclinical evaluation. Performance was also compared to the PSA reference device. This portion of the study included determination of analytical sensitivity, reproducibility and system calibration stability. Results were consistent with those observed in the

studies performed as part of the nonclinical evaluation and were equivalent to those obtained from the PSA reference device.

Correlation of the aca® *plus* PSA immunoassay test kit to an FDA Approved Assay

PSA values determined by the aca® ***plus*** PSA Test Kit were compared to PSA values obtained using a commercially available device for which there is an approved PMA (the reference device). The values obtained from the aca® ***plus*** PSA Test Kit were plotted for all subjects against the PSA values obtained with the reference device. The aca® ***plus*** PSA Test Kit compared with the reference device in all healthy and disease state categories and was consistent with the clinical status of the patient. A summary of the least squares regression analyses for samples within the assay range of 0-100 ng/mL is presented in Table 8.

Table 8 Summary of correlation versus the PSA reference device values within assay range

Site	n	Slope	Intercept	r	Sy,x
Site 1	980	0.97 ± 0.003	-0.15 ± 0.04	0.995	1.11
Site 2	887	1.00 ± 0.003	0.14 ± 0.04	0.996	1.09
Site 3	772	0.99 ± 0.003	0.03 ± 0.03	0.997	0.76
Pooled	**2639**	**0.98 ± 0.002**	**-0.0004±0.02**	**0.995**	**1.04**

Distribution of PSA Values and Concordance with Clinical Status

The distribution of PSA values observed for the aca® ***plus*** PSA Test Kit is presented in Table 9. The number of subjects and the percentage of those subjects within a given PSA range are shown for each healthy and disease state category.

The distribution of PSA values in subjects observed in this study as determined by the aca® ***plus*** PSA Test Kit was consistent with published values reported in current literature and with the clinical status of the patient.[7,16]

Table 9 Distribution of aca® ***plus*** PSA Values Summary

Patient Diagnosis	Number of Subjects	Percent (%)				
		0-4.0 ng/mL	4.1-10 ng/mL	10.1-30 ng/mL	30.1-60 ng/mL	>60 ng/mL
Healthy Subjects						
Males ≥40yrs	345	93.0	7.0	0.0	0.0	0.0
Males <40yrs	215	100.0	0.0	0.0	0.0	0.0
Females	93	100.0	0.0	0.0	0.0	0.0
Malignant Diseases						
Prostate						
Stage A	127	50.4	31.5	16.5	0.8	0.8
Stage B	300	51.0	30.7	15.3	2.3	0.7
Stage C	211	44.6	21.3	25.1	4.7	4.3
Stage D	275	29.8	10.9	15.6	9.1	34.6
Gastrointestinal	186	94.6	3.2	2.2	0.0	0.0
Genitourinary	136	93.4	4.4	2.2	0.0	0.0
Pulmonary	101	29.8	4.0	2.0	0.0	0.0
Non-malignant Diseases						
BPH	425	68.7	23.3	6.8	0.7	0.5
Prostatitis	35	74.3	20.0	5.7	0.0	0.0
Genitourinary	121	85.1	9.1	4.1	1.7	0.0
Hepatic	88	96.6	3.4	0.0	0.0	0.0
Renal	60	93.4	3.3	3.3	0.0	0.0

Clinical Utility as Demonstrated by Serial Samples

To confirm the utility of the aca® ***plus*** PSA Test Kit as an aid in the management of patients when prostate cancer has been diagnosed, serial samples were tested from patients with the disease. The study was retrospective and included serum specimens collected from 149 patients with prostatic carcinoma who had been monitored prospectively for 2.3 months to 8.9 years. Performance of the aca® ***plus*** PSA Test Kit was compared to that of the PSA reference device.

These studies included samples from 64 patients from, Johns Hopkins Hospital; samples from 63 patients from M.D. Anderson Cancer Center; and samples from 22 patients from The University of Alabama at

Birmingham. Of the 149 patients with prostatic carcinoma, 4 patients initially presented with Stage A disease, 35 patients with Stage B disease, 36 patients with Stage C disease, and 74 patients with Stage D disease. Disease stages were based on the American Urologic System[18] with Stage A being an intracapsular tumor/not palpable; Stage B an intracapsular palpable tumor; Stage C being tumor extension beyond capsule and extension to neighboring organs; and Stage D being metastatic carcinoma with lymph node involvement.

The results of the studies are summarized as follows:

- Samples from 45 patients had PSA levels that decreased following effective therapy (surgery, radiation, hormonal or chemotherapy) and remained at or below 4 ng/mL.

- Samples from 52 patients had PSA levels that decreased to 4 ng/mL or less following effective therapy but later showed an increase in PSA values. Disease recurrence correlated with rising PSA values, and was confirmed by digital rectal exam, X-ray, bone scan, biopsy, and/or clinical status.

- Samples from 45 patients had PSA levels that were continuously elevated above 4 ng/mL, but falling PSA levels indicated effective response to therapy and rising PSA levels indicated a deterioration in clinical status.

- Samples from four patients had PSA levels that decreased following effective therapy and continued to decrease even though the clinical status was deteriorating and progressive metastasis was confirmed. Patients were thought to have non-PSA producing metastatic tumors.

- Samples from three patients had PSA levels that decreased following effective therapy and then showed a gradual increase in PSA values over time with no clinical evidence of disease recurrence during the study phase.

In 142 out of 149 cases (95.3 percent), PSA levels were in concordance with the clinical status of the patient. In 100 percent of the cases the profiles of rise or fall of the aca® ***plus*** PSA Test Kit were congruent to the PSA reference method. These studies demonstrated the utility of the aca® ***plus*** PSA Test Kit as an aid in the management of prostate cancer patients.

VIII. Conclusions Drawn from the Studies

The aca® ***plus*** PSA Test Kit demonstrated the ability to determine the concentration of PSA in human serum and to act as an aid in the management of prostate cancer patients.

Nonclinical studies demonstrated the purity and specificity of the antibodies used in the aca® ***plus*** PSA Test Kit and of the antigen used to manufacture aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control. Performance characteristics of the assay, including sensitivity, specificity, reproducibility, stability, linearity and recovery demonstrated acceptable performance for an assay of this type

In clinical studies, the aca® ***plus*** PSA Test Kit demonstrated the ability to track, over time, a patient's response to therapy as shown by regression, remission, or recurrence of the cancer. Results of serial monitoring studies in 149 patients monitored for periods ranging from 2.3 months to 8.9 years established the efficacy of the aca® ***plus*** PSA Test Kit to act as an aid in the management of patients with prostate cancer.

The distribution of the PSA values as determined by the aca® ***plus*** PSA Test Kit demonstrated agreement usually seen in healthy individuals and patients with nonmalignant and malignant diseases. Results obtained from the serial monitoring study demonstrated satisfactory agreement between aca® ***plus*** PSA values and the patients' clinical status, as determined by other clinical modalities. These data support the clinical utility of the aca® ***plus*** PSA Test Kit as an aid in the management of prostate cancer patients.

IX. Panel Recommendation

Pursuant to section 515 (c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Immunology Devices Advisory Panel meeting because the information in the PMA substantially duplicates information previously reviewed by this Panel.

X. CDRH Action on the Application

CDRH issued an approval order for the applicant's PMA for the aca® ***plus*** PSA Test Kit, aca® ***plus*** PSA Calibrator, aca® ***plus*** PSA Control September 9, 1996.

The applicant's manufacturing and control facilities were inspected on July 31, 1996, and the facilities were found to be in compliance with the Good Manufacturing Practice Regulations (GMP's). The shelf-life of the aca® ***plus*** PSA Test Kit has been established at twelve months at 2-8°C. The shelf-life for the aca® ***plus*** PSA Calibrator and aca® ***plus*** PSA Control has been established for six months at 2-8°C.

XI. Approval Specifications

Directions for use: See attached labeling

Conditions of Approval: CDRH approval of this PMA is subject to full compliance with the conditions described in the approval order (Attachment B).

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aca® discrete clinical analyzer Test Methodology

PSA

PROSTATE SPECIFIC ANTIGEN

CAUTION: United States Federal law restricts this device to sale and distribution by or on the order of a physician or to a clinical laboratory and use is restricted to, by or on the order of a physician.

WARNING: The concentration of PSA in a given specimen, determined with assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the PSA assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining PSA levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

The aca®*plus* PSA assay should not be used for screening or early diagnosis of patients suspected to have prostate cancer. Untreated patients with prostate cancer may have serum levels of PSA within the range observed for apparently healthy individuals.[1] A low level of PSA does not necessarily indicate the absence of prostate cancer, particularly after therapeutic intervention such as surgery, irradiation, hormone therapy or chemotherapy.[2] Conversely, patients with nonmalignant prostate disease may have abnormal serum levels in the range observed for patients with prostate cancer.[2,3] An erroneously elevated PSA level can also be observed if the serum specimen from a patient is collected following digital rectal examination (DRE), needle biopsy or transurethral resection.[4,5] Therefore, serum PSA levels should be determined before any such procedure(s). For accurate determination of the PSA value, retesting for the PSA level should be delayed to allow the clearance of any PSA released due to these procedure(s).[5]

Patient samples may contain human anti-mouse antibodies (HAMA) that could give falsely elevated or depressed results with assays that use mouse monoclonal antibodies. This assay has been designed to minimize interference from HAMA containing samples.[7] No interference was observed in 78 HAMA-positive samples when tested with the aca®*plus* PSA assay.

Patients with a very high concentration of PSA may give a falsely low signal resulting in reporting of a suppressed PSA value. This artifact, called prozone reaction or high dose hook effect, is characteristic of two-site, one-step immunoassays.[8] Although PSA values seldom exceed 15,000 ng/mL, samples as high as 50,000 ng/mL have been tested in the aca®*plus* PSA assay. No hook effect was observed at this level of PSA.

Prostate cancer patients being treated with anti-androgens and LHRH agonists may show lower levels of PSA in serum.[9] Benign prostatic hypertrophy (BPH) patients treated with inhibitors of 5 alpha-reductase (finasteride) may also show reduction in their PSA values compared to values prior to treatment.[10]

INTENDED USE: The PSA test pack and reaction vessel are used in the aca® *plus* immunoassay system to quantitatively measure prostate specific antigen (PSA) in human serum. Measurements of PSA are used as an aid in the management of prostate cancer patients.

SUMMARY: Prostate specific antigen (PSA) is a serine protease of approximately 30,000 Daltons produced by the epithelial cells of the prostate gland.[11,12] PSA is found in high concentrations in seminal fluid and serves to liquefy the seminal coagulum.[13] The level of PSA in serum and other tissues is normally very low. In malignant prostate disease (prostatic adenocarcinoma) and in non-malignant disorders such as benign prostate hypertrophy (BPH) and prostatitis, the serum level of PSA may become elevated.[2,3,14,15] The specificity of PSA to prostate tissue makes it a significant marker in the management of prostate diseases.

Serum levels of PSA are most useful when sequential values are obtained and monitored over time. After complete removal of the prostate gland (radical prostatectomy), PSA levels should decline to a very low or undetectable level. A rise of the serum PSA level in prostatectomy patients indicates residual prostate tissue, recurrence or metastasis of the disease.[16] Serum PSA levels during radiation treatment should decline and remain at baseline while the patient is in remission.[17]

Recent research has demonstrated that most of the PSA protein in serum is complexed with either α_1-antichymotrypsin (ACT) or α_2-macroglobulin.[18,19] The PSA protein associated with α_2-macroglobulin is encapsulated and unavailable for measurement by current immunoassays. About 90% of the PSA in serum exists as PSA-ACT complex and 10% is free. The aca® *plus* PSA immunoassay is standardized with PSA-ACT and measures both the free and ACT bound components of serum PSA.

PSA testing is not recommended as a screening procedure in the general population nor as a guide in disease staging; however, it is accepted as an adjunctive test in the management of prostate cancer.[16,17]

PRINCIPLES OF PROCEDURE: The PSA method for the aca® *plus* immunoassay system is a one-step enzyme immunoassay based on the "sandwich" principle. The aca® *plus* mixes sample with chromium dioxide particles, coated with monoclonal antibodies specific for a binding site on PSA, and conjugate reagent (β-galactosidase labelled monoclonal antibodies specific for a second binding site on the PSA molecule).

A particle/PSA/conjugate sandwich forms during the incubation period. The aca® *plus* washes the sandwich to remove unbound conjugate and transfers the sandwich into a PSA test pack. The test pack is then placed onto an aca® analyzer for quantitation of PSA in the sample. The bound β-galactosidase catalyzes hydrolysis of chlorophenol red-β-D-galactopyranoside (CPRG) to chlorophenol red (CPR). The color change measured at 577 nm due to formation of CPR is directly proportional to the concentration of PSA present in the patient sample.

30

Cat. No. 791426901

DADE

aca®*plus* immunoassay system

Prostate Specific Antigen Calibrator

Intended Use
The aca®*plus* PSA Calibrator (Cat.# 791426901) is intended to be used on the aca®*plus* immunoassay system to calibrate the aca®*plus* Prostate Specific Antigen (PSA) method. This product was designed to meet the needs of users to assure accurate results over the assay range of this method.

Constituents
The aca®*plus* PSA Calibrator is a liquid product. Calibrator levels 2 and 3 contain human prostate specific antigen conjugated to α_1-Antichymotrypsin (PSA-ACT) in a bovine serum albumin base. Calibrator level 1 is a horse serum base with no detectable PSA-ACT. It is packaged as six vials, two at each level, 3 mL each.

Precautions
Irritant. Level 1 contains horse serum. May cause sensitization by skin contact. Avoid contact with skin. Wear suitable gloves.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead pipes in drain lines to form explosive compounds. Proper disposal of this product as a biohazard will minimize this possibility.

Contains human source material. When available a blood sample from the donor was tested and found negative for the presence of the antibody to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2), for Hepatitis B surface antigen (HBsAg), and for the antibody to Hepatitis C Virus (HCV). Where no donor blood sample was available, an extract of the starting material was tested and found negative for HIV-1, HIV-2, HBsAg, and HCV. Because no test can offer complete assurance that HIV-1, HIV-2, Hepatitis B or C virus, or other infectious agents are absent, this material should be handled using good laboratory practice to avoid skin contact and ingestion. Manuals are available which detail laboratory biosafety level criteria and practices.[1]

For *in vitro* diagnostic use.

Preparation
Allow to equilibrate to room temperature (22 - 28°C) and invert to mix before use.

Storage
Store at 2 - 8°C before and after opening.

Stability:
Unopened Vials: See Expiration Date.
Opened Vials: Once opened, assigned values are stable for 3 months when stored securely capped at 2 - 8°C between use.

Calibration Procedure
Refer to the manual supplied with the aca®*plus* system for calibration instructions.

Lot: XXXXXX

Exp.: XX XXX XX

	Constituent	Assigned Value[a,b]	Units	[S.I.] Units[c]
Level 1	PSA	X.X	ng/mL	[µg/L]
Level 2	PSA	XX.X	ng/mL	[µg/L]
Level 3	PSA	XXX.X	ng/mL	[µg/L]

a. The assigned values of PSA Calibrator are referenced to a Human Serum Master Pool. The assigned values are the means of multiple replicate determinations on several aca®*plus* systems, and have been confirmed by independent laboratories. All aca®*plus* systems were operating within instrument and temperature specifications.
b. Users of this product will be notified if there is a change in the assigned value.
c. Système International d'Unités.

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Dade International Inc.
Newark, DE 19714, U.S.A.

8/31/96 Rev. A PN 791426.100

Cat. No. 791426901

DADE

aca®*plus* immunoassay system

Calibrador del Antigeno Especifico de la Próstata

Uso
El calibrador de PSA para aca®*plus* (Ref. 791426901) se utiliza para calibrar el método del Antígeno Específico de la Próstata (PSA) en el sistema de inmunoensayo aca®*plus*. Este producto ha sido diseñado para satisfacer las necesidades del usuario en la obtención de resultados exactos en todo el rango analítico de este método.

Constituyentes
El calibrador de PSA para aca®*plus* es un producto líquido. Los niveles 2 y 3 del calibrador contienen Antígeno Específico de la Próstata humano conjugado a α_1-Antiquimiotripsina (PSA-ACT) en una base de albúmina de suero bovino. El nivel 1 del calibrador es suero de caballo con una cantidad *no* detectable de PSA-ACT. Consta de seis viales, dos de cada nivel, 3 mL por nivel.

Precauciones
Irritante. El nivel 1 contiene suero de caballo. Posibilidad de sensibilización en contacto con la piel. Evítese el contacto con la piel. Usense guantes adecuados.

Contiene azida sódica como conservante. La azida sódica puede reaccionar con el cobre o el plomo de las tuberías formando compuestos explosivos. Desechar de forma adecuada este producto como material biopeligroso minimizará esta posibilidad.

Contiene material de procedencia humana. Cuando estuvo disponible, una muestra de sangre del donante fue analizada y se encontró que era negativa para la presencia de anticuerpos contra el Virus de la Inmunodeficiencia Humana Tipo1 (HIV-1) y Tipo 2 (HIV-2), para el Antígeno de Superficie de la Hepatitis B (HBsAg), y para la presencia de anticuerpos contra el Virus de la Hepatitis C (HCV). Cuando no hubieron muestras de donantes disponibles, un extracto del material de inicio fue analizado, siendo negativo para HIV-1, HIV-2, HBsAg y HCV. Debido a que ningún test puede asegurar la ausencia de HIV-1 y HIV-2, virus de la Hepatitis B ó C, u otros agentes infecciosos, este material debe manejarse usando buenas prácticas de laboratorio para evitar el contacto con la piel o la ingestión. Hay manuales disponibles en los que se detalla el criterio de nivel de bioseguridad y su práctica en el laboratorio.[1]

Para uso de diagnostico *in vitro*.

Preparación
Dejar equilibrar los viales a temperatura ambiente (22 - 28°C) e invertir suavemente antes de su uso.

Conservación
Almacenar a 2 - 8°C antes y después de abrir.

Estabilidad
Viales sin abrir: Ver fecha de caducidad.
Viales abiertos: Una vez abiertos, los valores asignados son estables 3 meses cuando se guardan herméticamente cerrados a 2 - 8°C.

Procedimiento de Calibración
Referirse al manual suministrado con el sistema de inmunoensayo aca®*plus* para las instrucciones de calibración.

Lote: XXXXXX

Cód.: XX XXX XX

	Constituyente	Valor Asignado[a,b]	Unidades	Unidades [S.I.][c]
Nivel 1	PSA	X.X	ng/mL	[µg/L]
Nivel 2	PSA	XX.X	ng/mL	[µg/L]
Nivel 3	PSA	XXX.X	ng/mL	[µg/L]

a. Los valores asignados del calibrador de PSA están referidos a un Master Pool de sueros humanos. Los valores asignados son las medias de múltiples determinaciones realizadas en varios sistemas aca®*plus* y han sido confirmadas por laboratorios independientes. Todos los sistemas aca®*plus* trabajaron siguiendo las especificaciones de temperatura y de funcionamiento del instrumento.
b. Se informará a los usuarios de este producto si existe algún cambio en el valor asignado.
c. Système International d'Unités.

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8/31/96 Rev. A PN 791426.100

Cat. No. 791426901

DADE

aca® *plus* immunoassay system

Calibratore per Antigene Prostatico Specifico

Utilizzazione
Il Calibratore PSA aca® *plus* (Cod. 791426901) è un prodotto per uso diagnostico *in vitro*, il cui uso è previsto per la calibrazione del metodo Antigene Prostatico Specifico (PSA) sull' aca® *plus* immunoassay system. Questo prodotto è stato specificamente studiato per soddisfare le esigenze degli utilizzatori onde garantire risultati accurati nell'ampio intervallo di misura tipico del metodo.

Costituenti
Il Calibratore per PSA è un prodotto liquido. I livelli 2 e 3 contengono l'Antigene Specifico Prostatico di origine umana coniugato alla α_1-Antichimotripsina (PSA-ACT) in un siero bovino a base di albumina. Il livello 1 del Calibratore è un siero equino senza PSA-ACT. Il prodotto è costituito da sei flaconi, due per ciascun livello, 3 ml ciascuno.

Precauzioni
Irritante. Il livello 1 contiene siero equino. Può provocare sensibilizzazione per contatto con la pelle. Evitare il contatto con la pelle. Usare guanti adatti.

Contiene sodio azoturo come conservante. I sodio azoturo può reagire con le tubature in rame o piombo dei condotti di scarico con formazione di composti esplosivi. Questa possibilità è minimizzata dallo smaltimento di questo prodotto con le procedure riservate ai materiali portatori di potenziale rischio biologico.

Contiene materiale di origine umana. Ciascun donatore utilizzato nella preparazione di questo prodotto è stato controllato per la presenza dell'anticorpo contro il virus dell'immunodeficienza umana di tipo1 (HIV-1) e di tipo 2 (HIV-2), dell'antigene di superficie dell'epatite B (HBsAg) e del virus dell'epatite C (HCV), risultando negativo (ripetutamente non reattivo). Quando non è stato possibile utilizzare alcun donatore, l' estratto della matrice utilizzata è stato comunque controllato per HIV-1, HIV-2, HBsAg e HCV, risultando negativo. Poiché nessun metodo può garantire con assoluta sicurezza che questi o altri agenti infettanti siano assenti, questo materiale dovrebbe essere trattato usando le basilari precauzioni della pratica di laboratorio per evitare il contatto con la pelle e l'ingestione. Sono disponibili manuali che descrivono i gradi e le procedure della sicurezza biologica del laboratorio.[1]

Per uso diagnostico *in vitro*.

Procedura
Lasciare ad equilibrare a temperatura ambiente (22 - 28°C) e capovolgere prima dell'uso.

Conservazione
Conservare a 2 - 8°C prima e dopo la ricostituzione.

Stabilità
Flacone chiuso: Vedere data di scadenza.
Flacone aperto: Una volta aperti i flaconi, i valori assegnati sono stabili per 3 mesi quando i flaconi sono conservati ben chiusi a 2 - 8°C.

Procedura di Calibrazione
Fare riferimento al manuale fornito con l' aca® *plus* per le istruzioni di calibrazione e verifica.

Lotto: XXXXX

Scadenza.: XX XXX XX

	Analita	Valore Assegnato[a,b]	Unità	Unità (S.I.)[c]
Livello 1	PSA	X.X	ng/ml	[µg/l]
Livello 2	PSA	XX.X	ng/ml	[µg/l]
Livello 3	PSA	XXX.X	ng/ml	[µg/l]

a. I valori assegnati del Calibratore PSA sono riferiti ad un Pool di riferimento di Siero Umano. I valori assegnati sono la media di determinazioni replicate su diversi sistemi aca® *plus* e sono state confermate da laboratori indipendenti. Tutti i sistemi aca® *plus* hanno lavorato entro le specifiche dello strumento e di temperatura.
b. Gli utilizzatori di questo prodotto saranno avvertiti in caso di cambiamenti nei Valori Assegnati.
c. Système International d'Unités.

Bibliografia
1. Biosafety in Microbiological and Biomedical Laboratories, HHS Publication No. (CDC) 88-8395, Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

Dade S.p.A.
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8/31/96 Rev. A PN 791426.100

Cat. No. 791426901

DADE

aca®*plus* immunoassay system

Etalon Antigène Spécifique de la Prostate

Utilisation
L'Etalon PSA aca®*plus* (Cat 791426901) est destiné à *étalonner* la méthode Antigène Spécifique de la Prostate (PSA) sur le système d'immunodosage aca®*plus*. Ce produit a été conçu pour assurer des résultats exacts sur toute l'étendue du domaine de mesure de cette méthode.

Composition
L'Etalon PSA aca®*plus* est un produit liquide. Les étalons des niveaux 2 et 3 contiennent de l'Antigène Spécifique de la Prostate conjugué à de l' α_1-Antichymotrypsine (PSA-ACT) dans une base de sérum albumine bovine. Le niveau 1 est à base de sérum de cheval avec du PSA-ACT non détectable. La boîte contient six flacons, deux par niveau, 3 ml chacun.

Précautions
Irritant. Le niveau 1 contient du serum de cheval. Peut entraîner une sensibilisation par contact avec le peau. Eviter le contact avec la peau, porter des gants appropriés.

Contient de l'azide de sodium comme conservateur. L'azide de sodium peut réagir avec des canalisations en cuivre ou en plomb pouvant former des mélanges explosifs. Une élimination appropriée de ce produit biologiquement dangereux amenuisera cette possibilité.

Contient un produit d'origine humaine. Quand un échantillon de sang du donneur était disponible, celui-ci a été testé et trouvé négatif pour la présence de l'anticorps vis-à-vis du virus de l'Immunodéficience Humaine Type 1 (HIV-1) et de Type 2 (HIV-2), de l'antigène de surface du virus de l'Hépatite B (HBsAg), et des anticorps vis-à-vis du virus de l'hépatite C (HCV). Quand un échantillon de sang n'était pas disponible, un extrait de la matière première a été testé et trouvé négatif pour HIV-1, HIV-2, HBsAg et HCV. Du fait qu'aucun test ne peut offrir une assurance complète que les virus HIV-1 et HIV-2 et des Hépatites B ou C ou que d'autres agents infectieux sont absents, ce produit doit être manipulé en respectant une Bonne Pratique de Laboratoire pour éviter le contact avec la peau et l'ingestion. Des manuels détaillant la sécurité biologique au laboratoire, ses critères, ses pratiques.

Pour usage diagnostic *in vitro*.

Preparation
Laisser équilibrer à la température ambiante (22 - 28°C) et agiter doucement par retournements pour mélanger avant l'utilisation.

Conservation
Conserver à 2 - 8°C avant et après ouverture.

Stabilité
Flacons non ouverts: Voir date d'expiration.
Flacons ouverts: Une fois flacons ouverts, les valeurs attribuées sont stables 3 mois lorsque ceux-ci sont soigneusement fermés et conservés à 2 - 8°C entre chaque usage.

Procédure d'Etalonnage
Se reporter au manuel d'utilisation du système d'immunodosage aca®*plus* pour les instructions d'étalonnage.

Lot: XXXXXX

Exp.: XX XXX XX

	Composition	Valeur Attribuée[a,b]	Unités	Unités [S.I.][c]
Niveau 1	PSA	X.X	ng/ml	[µg/l]
Niveau 2	PSA	XX.X	ng/ml	[µg/l]
Niveau 3	PSA	XXX.X	ng/ml	[µg/l]

a. Les valeurs attribuées de l'étalon PSA sont référencées à un Pool Maître de sérums humains. Les valeurs attribuées sont la moyenne de déterminations multiples sur plusieurs systèmes aca®*plus* et ont été confirmées par des laboratoires indépendants. Les systèmes aca®*plus* répondaient aux spécifications de l'instrument et de la température.
b. Les utilisateurs de ce produit seraient avertis si les valeurs attribuées changeaient.
c. Système International d'Unités.

Bibliographie
1. Biosafety in Microbiological and Biomedical Laboratories, HHS Publication No. (CDC) 88-8395, Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

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Cat. No. 791426901

DADE

aca®*plus* immunoassay system

Prostataspezifisches Antigen Kalibrator

GEBRAUCHSINFORMATION

Verwendungszweck
Der aca®*plus* PSA Kalibrator (Kat. Nr. 791426901) wird auf dem Immunoassay System aca®*plus* zur Kalibrierung der aca®*plus* Methode Prostataspezifisches Antigen (PSA) verwendet. Der Kalibrator stellt sicher, daß genaue Ergebnisse über den gesamten Meßbereich dieser Methode erzielt werden.

Zusammensetzung
Der aca®*plus* PSA Kalibrator ist ein flüssiges Produkt. Kalibrator Level 2 und 3 enthalten humanes prostataspezifisches Antigen konjugiert mit α_1-Antichymotrypsin (PSA-ACT) in Rinderserumalbuminlösung. Kalibrator Level 1 besteht aus Pferdeserum mit nichtnachweisbaren Mengen PSA-ACT.

Inhalt: 6 Fläschchen, 3 Level, 2 Fläschchen pro Level mit je 3 ml.

Reizend. Level 1 enthält pferdeserum. Sensibilisierung durch hautkontakt möglich. Berührung mit der Haut vermeiden. Geeignete Schutzhandschuhe tragen.

Enthält Natriumazid als Konservierungsmittel. Natriumazid kann in Kupfer- oder Bleirohren von Abwasserleitungen explosive Verbindungen bilden.

Enthält Material menschlichen Ursprungs. Soweit vorhanden wurde eine Blutprobe des Gewebespenders auf Antikörper gegen das Human Immunodeficiency Virus Typ 1 und Typ 2 (HIV-1 und HIV-2), gegen Hepatitis B Oberflächenantigen (HBsAg) sowie auf das Vorhandensein von Antikörpern gegen das Hepatitis C Virus (HCV) getestet und für negativ befunden. Falls keine Blutprobe des Spenders zur Verfügung stand, wurde ein Extrakt des Ausgangsmaterials auf HIV, HBsAg und HCV getestet und für negativ befunden. Kein bekanntes Testverfahren kann jedoch gewährleisten, daß HIV-1, HIV-2, Hepatitis B oder C Viren oder andere infektiöse Agentien abwesend sind. Daher müssen diese Produkte mit angemessener Sorgfalt unter Einhaltung der bei Biogefährdung empfohlenen Sicherheitsmabnahmen gehandhabt werden.

In vitro Diagnosticum.

Vorbereitung
Der Kalibrator sollte vor Gebrauch auf Raumtemperatur (22 - 28°C) gebracht und durch Kippen gemischt werden.

Lagerung
Vor und nach dem Rekonstituieren bei 2 - 8°C lagern

Haltbarkeit
Ungeöffnete Fläschchen: Siehe Verfalldatum.
Geöffnete Fläschchen: Einmal geöffnet bleiben die Sollwerte für 3 Monate stabil, wenn die Fläschchen zwischen den Anwendungen gut verschlossen bei 2 - 8°C gelagert werden.

Kalibrierverfahren
Ausführliche Erläuterungen finden Sie im Gerätehandbuch des Dade Immunoassay Systems aca®*plus*.

Ch.-B.: XXXXX

Verw. bis: XX XXX XX

	Bestandteil	Sollwert[a,b]	Einheiten	(SI)-Einheiten[c]
Level 1	PSA	X,X	ng/ml	[µg/l]
Level 2	PSA	XX,X	ng/ml	[µg/l]
Level 3	PSA	XXX,X	ng/ml	[µg/l]

a. Die Sollwerte des PSA Kalibrators beziehen sich auf einen Humanserum-Masterpool. Die Sollwerte sind Mittelwerte aus Mehrfachbestimmungen auf mehreren aca®*plus* Systemen und werden von unabhängigen Laboratorien bestätigt. Alle aca®*plus* Systeme arbeiteten innerhalb der Geräte- und Temperaturspezifikationen.
b. Anwender dieses Produktes werden benachrichtigt, wenn die Sollwerte sich ändern.
c. Système International d'Unités.

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8/31/96 Rev. A PN 791426.100

Cat. No. 791425901

DADE

aca®*plus* immunoassay system

Prostate Specific Antigen Control

Intended Use
The aca®*plus* PSA Control (Cat.# 791425901) is intended to be used on the aca®*plus* immunoassay system as a quality control product for the aca®*plus* Prostate Specific Antigen (PSA) method.

Constituents
The aca®*plus* PSA Control is a liquid product. Control levels 1 and 2 contain human prostate specific antigen conjugated to α_1-Antichymotrypsin (PSA-ACT) in a bovine serum albumin base. It is packaged as twelve vials, six at each level, 5 mL each.

Precautions
Contains sodium azide as a preservative. Sodium azide can react with copper or lead pipes in drain lines to form explosive compounds. Proper disposal of this product as a biohazard will minimize this possibility.

Contains human source material. When available a blood sample from the donor was tested and found negative for the presence of the antibody to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2), for Hepatitis B surface antigen (HBsAg), and for the antibody to Hepatitis C Virus (HCV). Where no donor blood sample was available, an extract of the starting material was tested and found negative for HIV-1, HIV-2, HBsAg, and HCV. Because no test can offer complete assurance that HIV-1, HIV-2, Hepatitis B or C virus, or other infectious agents are absent, this material should be handled using good laboratory practice to avoid skin contact and ingestion. Manuals are available which detail laboratory biosafety level criteria and practices.[1]

For *In vitro* diagnostic use.

Preparation
Allow to equilibrate to room temperature (22 - 28°C) and invert to mix before use.

Storage
Store at 2 - 8°C before and after opening.

Stability
Unopened Vials: See Expiration Date.
Opened Vials: Once opened, controls are stable for 3 months when stored securely capped at 2 - 8°C between use.

Lot: XXXXXX

Exp.: XX XXX XX

	Constituent	Expected Range[a,b,c]	Units	[S.I.] Units[d]
Level 1	PSA	X.X - X.X	ng/mL	[µg/L]
Level 2	PSA	XX.X - XX.X	ng/mL	[µg/L]

a. The expected ranges of PSA Control are referenced to a Human Serum Master Pool. The ranges represent target intervals for the means of multiple replicate determinations on several aca®*plus* systems. All aca®*plus* systems were operating within instrument and temperature specifications.
b. Individual laboratory means should fall within the expected ranges. At each level of quality control, the laboratory should establish its own range and use the expected range provided only as a guide. Refer to the Chemistry Guide supplied with the aca® discrete clinical analyzer for Quality Control information.
c. Users of this product will be notified if there is a change in the expected range.
d. Système International d'Unités.

Bibliography
1. Biosafety in Microbiological and Biomedical Laboratories, HHS Publication No. (CDC) 88-8395. Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

Dade International Inc.
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8/31/96 Rev. A PN 791425.100

34

Cat. No. 791425901

DADE

aca®*plus* immunoassay system

Control del Antigeno Especifico de la Próstata

Uso
El control de PSA para aca®*plus* (Ref. 791425901) se utiliza como material de control de calidad del método del Antígeno Específico de la Próstata (PSA) en el sistema de inmunoensayo aca®*plus*.

Constituyentes
El control de PSA para aca®*plus* es un producto líquido. Los niveles 1 y 2 del control contienen Antígeno Específico de la Próstata humano conjugado a α_1-Antiquimiotripsina (PSA-ACT) en una base de albúmina de suero bovino. Consta de doce viales, seis de cada nivel, 5 mL por nivel.

Precauciones
Contiene azida sódica como conservante. La azida sódica puede reaccionar con el cobre o el plomo de las tuberías formando compuestos explosivos. Desechar de forma adecuada este producto como material biopeligroso minimizará esta posibilidad.

Contiene material de procedencia humana. Cuando estuvo disponible, una muestra de sangre del donante fue analizada y se encontró que era negativa para la presencia de anticuerpos contra el Virus de la Inmunodeficiencia Humana Tipo1 (HIV-1) y Tipo 2 (HIV-2), para el Antígeno de Superficie de la Hepatitis B (HBsAg), y para la presencia de anticuerpos contra el Virus de la Hepatitis C (HCV). Cuando no hubieron muestras de donantes disponibles, un extracto del material de inicio fue analizado, siendo negativo para HIV-1, HIV-2, HBsAg y HCV. Debido a que *ningún* test puede asegurar la ausencia de HIV-1 y HIV-2, virus de la Hepatitis B ó C, u otros agentes infecciosos, este material debe manejarse usando buenas prácticas de laboratorio para evitar el contacto con la piel o la ingestión. Hay manuales disponibles en los que se detalla el criterio de nivel de bioseguridad y su práctica en el laboratorio.[1]

Para uso de diagnostico *in vitro*.

Preparación
Dejar equilibrar los viales a temperatura ambiente (22 - 28°C) e invertir suavemente antes de su uso.

Conservación
Almacenar a 2 - 8°C antes y después de abrir.

Estabilidad
Viales *sin* abrir: Ver fecha de caducidad.
Viales abiertos: Una vez abiertos, los controles son estables 3 meses cuando se guardan herméticamente cerrados a 2 - 8°C.

Lote: XXXXX

Cad.: XX XXX XX

	Constituyente	Rango Esperado[a,b,c]	Unidades	Unidades (S.I.)[d]
Nivel 1	PSA	X.X - X.X	ng/mL	(µg/L)
Nivel 2	PSA	XX.X - XX.X	ng/mL	(µg/L)

a. Los rangos esperados del control de PSA están referidos a un Master Pool de sueros humanos. El rango son las medias de los intervalos de múltiples determinaciones en varios sistemas aca®*plus*. Todos los sistemas aca®*plus* estuvieron trabajaron dentro las especificaciones de funcionamiento y temperatura del instrumento.
b. Las medias de cada laboratorio individual, deberían estar dentro de los rangos esperados. Para cada nivel del control, el laboratorio debería establecer su propio rango y solamente utilizar el rango esperado como una guía. Refiérase al Manual de Métodos que se suministra con el aca®*plus* para más información sobre control de calidad.
c. Se informará a los usuarios de este producto si existe algún cambio en el rango esperado.
d. Système International d'Unités.

Bibliografía
1. Biosafety in Microbiological and Biomedical Laboratories. HHS Publication No. (CDC) 88-8395. Superintendent of Documents, U.S. Government Printing Office., Washington, DC 20402.

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8/31/96 Rev A PN 791425.100

37

Cat. No. 791425901

DADE

aca®*plus* immunoassay system

Prostataspezifisches Antigen Kontrolle

GEBRAUCHSINFORMATION

Verwendungszweck
Die aca®*plus* PSA Kontrolle (Kat. Nr. 791425901) wird auf dem Immunoassay System aca®*plus* zur Qualitätskontrolle der aca®*plus* Methode Prostataspezifisches Antigen (PSA) verwendet.

Zusammensetzung
Die aca®*plus* PSA Kontrolle ist ein flüssiges Produkt. Kontrolle Level 1 und 2 enthalten humanes prostataspezifisches Antigen konjugiert mit α_1-Antichymotrypsin (PSA-ACT) in Rinderserumalbuminlösung.

Inhalt: 12 Fläschchen, 2 Level, 6 Fläschchen pro Level mit je 5 ml.

Vorsicht
Enthält Natriumazid als Konservierungsmittel. Natriumazid kann in Kupfer- oder Bleirohren von Abwasserleitungen explosive Verbindungen bilden.

Enthält Material menschlichen Ursprungs. Soweit vorhanden wurde eine Blutprobe des Gewebespenders auf Antikörper gegen das Human Immunodeficiency Virus Typ 1 und Typ 2 (HIV-1 und HIV-2), gegen Hepatitis B Oberflächenantigen (HBsAg) sowie auf das Vorhandensein von Antikörpern gegen das Hepatitis C Virus (HCV) getestet und für negativ befunden. Falls keine Blutprobe des Spenders zur Verfügung stand, wurde ein Extrakt des Ausgangsmaterials auf HIV, HBsAg und HCV getestet und für negativ befunden. Kein bekanntes Testverfahren kann jedoch gewährleisten, daß HIV-1, HIV-2, Hepatitis B oder C Viren oder andere infektiöse Agentien abwesend sind. Daher müssen diese Produkte mit angemessener Sorgfalt unter Einhaltung der bei Biogefährdung empfohlenen Sicherheitsmaßnahmen gehandhabt werden.

In vitro Diagnosticum.

Vorbereitung
Die Kontrolle sollte vor Gebrauch auf Raumtemperatur (22 - 28°C) gebracht und durch Kippen gemischt werden.

Lagerung
Vor und nach dem Rekonstituieren bei 2 - 8°C lagern.

Haltbarkeit:
Ungeöffnete Fläschchen: Siehe Verfalldatum.
Geöffnete Fläschchen: Einmal geöffnet bleiben die Kontrollen für 3 Monate stabil, wenn die Fläschchen zwischen den Anwendungen gut verschlossen bei 2 - 8°C gelagert werden.

Ch.-B.: XXXXX

Verw. bis: XX XXX XX

	Bestandteil	Sollwertbereich[a,b,c]	Einheiten	(SI)-Einheiten[d]
Level 1	PSA	X.X - X.X	ng/ml	(µg/l)
Level 2	PSA	XX.X - XX.X	ng/ml	(µg/l)

a. Die Sollwertbereiche der PSA Kontrolle beziehen sich auf einen Humanserum-Masterpool. Die Sollwertbereiche sind Zielwerte für die Mittelwerte wiederholter Mehrfachbestimmungen auf mehreren aca®*plus* Systemen. Alle aca®*plus* Systeme arbeiteten innerhalb der Geräte- und Temperaturspezifikationen.
b. Die Mittelwerte eines individuellen Labors sollten in diesen Bereich fallen. Für jeden Level der Qualitätskontrolle sollte das Labor seinen eigenen Bereich festlegen, die publizierten Bereiche sollen nur als Anhalt dienen. Siehe Chemiehandbuch für Informationen zur Qualitätskontrolle.
c. Anwender dieses Produktes werden benachrichtigt, falls sich die Bereiche ändern.
d. Système International d'Unités.

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38

Cat. No. 791425901

DADE

aca®*plus* immunoassay system

Controle Antigène Spécifique de la Prostate

Utilisation
Le Contrôle PSA aca®*plus* (Cat 791425901) est destiné à être utilisé sur le système d'immunodosage aca®*plus* en tant que contrôle de qualité de la méthode Antigène Spécifique de la Prostate (PSA).

Composition
Le Contrôle PSA aca®*plus* est un produit liquide. Les niveaux 1 et 2 du Contrôle contiennent de l'Antigène Spécifique de la Prostate conjugué à de l'α_1-Antichymotrypsine (PSA-ACT) dans une base de sérum albumine bovine. La boîte contient douze flacons, six par niveau, 5 ml chacun.

Précautions
Contient de l'azide de sodium comme conservateur. L'azide de sodium peut réagir avec des canalisations en cuivre ou en plomb pouvant former des mélanges explosifs. Une élimination appropriée de ce produit biologiquement dangereux amenuisera cette possibilité.

Contient un produit d'origine humaine. Quand un échantillon de sang du donneur était disponible, celui-ci a été testé et trouvé négatif pour la présence de l'anticorps vis-à-vis du virus de l'Immunodéficience Humaine Type 1 (HIV-1) et de Type 2 (HIV-2), de l'antigène de surface du virus de l'Hépatite B (HBsAg), et des anticorps vis-à-vis du virus de l'hépatite C (HCV). Quand un échantillon de sang n'était pas disponible, un extrait de la matière première a été testé et trouvé négatif pour HIV-1, HIV-2, HBsAg et HCV. Du fait qu'aucun test ne peut offrir une assurance complète que les virus HIV-1 et HIV-2 et des Hépatites B ou C ou que d'autres agents infectieux sont absents, ce produit doit être manipulé en respectant une Bonne Pratique de Laboratoire pour éviter le contact avec la peau et l'ingestion. Des manuels détaillant la sécurité biologique au laboratoire, ses critères, ses pratiques.

Pour usage diagnostic *in vitro*.

Preparation
Laisser équilibrer à la température ambiante (22 - 28°C) et agiter doucement par retournements pour mélanger avant l'utilisation.

Conservation
Conserver à 2 - 8°C avant et après ouverture.

Stabilité
Flacons non ouverts: Voir date d'expiration.
Flacons ouverts: Une fois flacons ouverts, les contrôles sont stables 3 mois lorsque ceux-ci sont soigneusement fermés et conservés à 2 - 8°C entre chaque usage.

Lot: XXXXXX

Exp.: XX XXX XX

	Composition	Intervalle Attendu[a,b,c]	Unités	Unités [S.I.][d]
Niveau 1	PSA	X.X - X.X	ng/ml	(µg/l)
Niveau 2	PSA	XX.X - XX.X	ng/ml	(µg/l)

a. Les intervalles attendus pour le Contrôle PSA sont référencés à un Pool Maître de sérums humains. Les intervalles représentent les cibles des moyennes de multiples déterminations sur plusieurs systèmes aca®*plus*. Les systèmes aca®*plus* répondaient aux spécifications de l'instrument et de la température.
b. Les moyennes individuelles des laboratoires doivent se situer dans les intervalles attendus. A chaque niveau de contrôle de qualité, le laboratoire doit établir ses propres intervalles attendus et utiliser celles qui sont fournies comme guide. Se reporter au manuel de chimie de l'analyseur aca pour plus d'information sur le Contrôle de Qualité.
c. Les utilisateurs de ce produit seraient avertis si les intervalles attendus changeaient.
d. Système International d'Unités.

Bibliographie
1. Biosafety in Microbiological and Biomedical Laboratories, HHS Publication No. (CDC) 88-8395, Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

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8/31/96 Rev. A PN 791425.1

Cat. No. 791425901

DADE

aca®*plus* immunoassay system

Controllo per Antigene Prostatico Specifico

Utilizzazione
Il Controllo PSA aca®*plus* (Cod. 791425901) è un prodotto per uso diagnostico *in vitro*, il cui uso è previsto sull'aca®*plus* come prodotto del controllo di qualità per il metodo Antigene Prostatico Specifico (PSA) sull' aca®*plus* immunoassay system.

Costituenti
Il Controllo per PSA è un prodotto liquido. I livelli 1 e 2 contengono l'Antigene Specifico Prostatico di origine umana coniugato alla α_1-Antichimotripsina (PSA-ACT) in un siero bovino a base di albumina. Il prodotto è costituito da dodici flaconi, sei per ciascun livello, 5 ml ciascuno.

Precauzioni
Contiene sodio azoturo come conservante. Il sodio azoturo può reagire con le tubature in rame o piombo dei condotti di scarico con formazione di composti esplosivi. Questa possibilità è minimizzata dallo smaltimento di questo prodotto con le procedure riservate ai materiali portatori di potenziale rischio biologico.

Contiene materiale di origine umana. Ciascun donatore utilizzato nella preparazione di questo prodotto é stato controllato per la presenza dell'anticorpo contro il virus dell'immunodeficienza umana di tipo1 (HIV-1) e di tipo 2 (HIV-2), dell'antigene di superficie dell'epatite B (HBsAg) e del virus dell'epatite C (HCV), risultando negativo (ripetutamente non reattivo). Quando non é stato possibile utilizzare alcun donatore, l' estratto della matrice utilizzata é stato comunque controllato per HIV-1, HIV-2, HBsAg e HCV, risultando negativo. Poiché nessun metodo può garantire con assoluta sicurezza che questi o altri agenti infettanti siano assenti, questo materiale dovrebbe essere trattato usando le basilari precauzioni della pratica di laboratorio per evitare il contatto con la pelle e l'ingestione. Sono disponibili manuali che descrivono i gradi e le procedure della sicurezza biologica del laboratorio.[1]

Per uso diagnostico *in vitro*.

Procedura
Lasciare ad equilibrare a temperatura ambiente (22 - 28°C) e capovolgere prima dell'uso.

Conservazione
Conservare a 2 - 8°C prima e dopo la ricostituzione.

Stabilità
Flacone chiuso: Vedere data di scadenza.
Flacone aperto: Una volta aperti i flaconi, i controlli sono stabili per 3 mesi quando i flaconi sono conservati ben chiusi a 2 - 8°C.

Lotto: XXXXXX

Scadenza.: XX XXX XX

	Analita	Intervallo Atteso[a,b,c]	Unità	Unità (S.I.)[d]
Livello 1	PSA	X.X - X.X	ng/ml	[µg/l]
Livello 2	PSA	XX.X - XX.X	ng/ml	[µg/l]

a. Gli intervalli attesi del Controllo PSA sono riferiti ad un Pool di riferimento di Siero Umano. Gli intervalli sono stati ottenuti dalla media di molte determinazioni replicate su diversi sistemi aca®*plus*. Tutti i sistemi aca®*plus* furono impiegati entro le specifiche dello strumento e della temperatura.
b. Le medie di ciascun laboratorio dovrebbero essere all'interno degli intervalli attesi. Ad ogni livello del controllo di qualità, il laboratorio dovrebbe stabilire il suo proprio intervallo ed utilizzare l'intervallo atteso solo come guida. Fare riferimento al Manuale di Chimica forniti con l'analizzatore clinico discreto aca® per informazioni sul Controllo di Qualità.
c. Gli utilizzatori di questo prodotto saranno avvertiti in caso di cambiamenti nell'intervallo atteso.
d. Système International d'Unités.

Bibliografia
1. Biosafety in Microbiological and Biomedical Laboratories. HHS Publication No. (CDC) 88-8395. Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

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